Claim 26 is amended to recite "caused all or in part by said deficiency in α-L-iduronidase". Amendment is made to further clarify that the "lysosomal storage" is "caused all or in part by said deficiency in α-L-iduronidase". Support for the amendent is found, for example, in Claim 14 as originally filed and page 1, lines 24-25.

Claim 28 is amended to recite "increase in percent forced vital capacity, increase in distance of six-minute walk, reduction of liver volume and urinary glycosaminoglycan excretion, reduction in spleen size and apnea/hypopnea events, increase in height and growth velocity in prepubertal patients, increase in shoulder flexion and elbow and knee extension, reduction in symptoms related to cardiac function, and increase in endurance and reduction of limitations of daily activities". Amendment is made to further clarify that the effects of the improvements and normalizations. Support for the amendent is found, for example, in page 33, line 16 to page 36, line 24.

Support for new Claim 29 is found, for example, from page 13, line 25 to page 14, line 35.

Support for new Claims 30, 31, 40 and 41 is found, for example, in page 5, line 25.

Support for new Claims 32 and 42 is found, for example, in page 5, lines 25-26.

Support for new Claims 33 and 43 is found, for example, in Claim 21 as originally filed.

Support for new Claims 34 and 44 is found, for example, in page 23, line 30.

Support for new Claims 35 and 45 is found, for example, in Claim 24 as originally filed.

Support for new Claims 36 and 46 is found, for example, in Claim 25 as originally filed.

Support for new Claims 37 and 47 is found, for example, in page 23,lines 19-20.

Support for new Claims 38 is found, for example, in page 33, line 16 to page 36, line 24.

Support for new Claims 39 is found, for example, in page 5, lines 17-20 and page 18, lines 16.

Support for new Claims 48 and 49 is found, for example, in page 34, lines 17-21.

Support for new Claim 50 is found, for example, in page 34, lines 21-23.

Support for new Claim 51 is found, for example, in page 34, lines 24-25.

Support for new Claim 52 is found, for example, in page 35, lines 1-3.

Support for new Claim 53 is found, for example, in page 35, lines 3-6.

Support for new Claim 54 is found, for example, in page 35, lines 7-9.

Support for new Claim 55 is found, for example, in page 35, lines 9-10.

Support for new Claim 56 is found, for example, in page 35, lines 18-20.

Support for new Claim 57 is found, for example, in page 35, lines 1-10.

No new matter is added in any of the above amendments and the Examiner is respectfully requested to enter the amendments.

Respectfully submitted,

Date: October 2, 2002

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Marked Up Version to Show Changes Made

In the Claims:

Please amend Claims 19, 21, 22, 24, 26 and 28 as follows:

19. (Amended) The method of Claim 14 wherein the disease is [MPS] mucopolysaccharidosis I.

21. (Amended) The method of Claim 14 wherein said human subject suffering from the disease demonstrates about 1% or less of a normal α-L-iduronidase activity.

22. (Amended) The method of Claim 14 wherein a dose of at least about 100 units per kilogram said human recombinant α-L-iduronidase is administered weekly to [a patient] said human subject suffering from [a] said deficiency [thereof].

24. (Amended) The method of Claim 14 wherein said administering is [the] a slow infusion of at least 0.5 mg/kg of said formulation for about an hour, followed by a rapid two-hour infusion rate.

26. (Amended) The method of Claim 14 wherein said treatment with human recombinant α-L-iduronidase reduces lysosomal storage caused all or in part by said deficiency in α-L-iduronidase.

28. (Amended) The method of Claim 14 wherein said treatment results in [improvement] increase in percent forced vital capacity, [improvement] increase in distance of six-minute walk, [normalization] reduction of liver volume and urinary glycosaminoglycan excretion, reduction in spleen size and apnea/hypopnea events, increase in height and growth velocity in prepubertal patients, [improvement] increase in shoulder flexion and elbow and knee extension, [improvement] reduction in symptoms related to cardiac function, and [improvement] increase in endurance and reduction of limitations of daily activities.

Please add the following new claims:

--29. (New) A method of treating diseases caused all or in part by a deficiency in α-L-iduronidase, comprising the steps of:

(a) administering a pharmaceutical composition comprising a purified human recombinant α-L-iduronidase, or biologically active fragment or mutein thereof, having a purity of greater than about 99%, to a human subject in need thereof; and

(b) optimizing said treatment by evaluating biochemical and clinical symptoms of said subject through routine assessment of history, physical examination, echocardiography, electrocardiography, magnetic resonance imaging, polysomnography, skeletal survey, range of motion measurements, corneal photographs, and skin biopsy.

30. (New) The method of Claim 29 wherein the disease is mucopolysaccharidosis.

31. (New) The method of Claim 29 wherein the disease is mucopolysaccharidosis I.

32. (New) The method of Claim 29 wherein the disease is selected from the group consisting of: Hurler's disease, Scheie syndrome and Hurler-Scheie syndrome.

33. (New) The method of Claim 29 wherein said subject suffering from the disease demonstrates about 1% or less of a normal α-L-iduronidase activity.

34. (New) The method of Claim 29 wherein a dose of at least about 125,000 units or 0.5 mg/kg of said human recombinant α-L-iduronidase is administered weekly to a patient suffering from a deficiency thereof

35. (New) The method of Claim 29 wherein said administering is a slow infusion of at least 0.5 mg/kg of said formulation for about an hour, followed by a rapid two-hour infusion rate.

36. (New) The method of Claim 29 wherein said infusion is used to minimize complement mediation clinical allergic reactions.

37. (New) The method of Claim 29 wherein said treatment with human recombinant α-L-iduronidase reduces lysosomal storage caused all or in part by said deficiency in α-L-iduronidase of said human subjects .

38. (New) The method of Claim 29 wherein said treatment results in normalization of liver volume and urinary glycosaminoglycan excretion, reduction in spleen size and apnea/hypopnea events, increase in height and growth velocity in prepubertal patients, increase in shoulder flexion and elbow and knee extension, and reduction in tricuspid regurgitation or pulmonic regurgitation.

39. (New) A method of treating diseases caused all or in part by a deficiency in α-L-iduronidase, comprising the steps of:

administering a pharmaceutical composition to a human subject in need thereof; wherein said pharmaceutical composition comprises a purified human recombinant α-L-iduronidase, or biologically active fragment or mutein thererof, having a purity of greater than about 99%.

40. (New) The method of Claim 39 wherein the disease is mucopolysaccharidosis.

41. (New) The method of Claim 39 wherein the disease is mucopolysaccharidosis I.

42. (New) The method of Claim 39 wherein the disease is selected from the group consisting of: Hurler's disease, Scheie syndrome and Hurler-Scheie syndrome.

43. (New) The method of Claim 39 wherein said subject suffering from the disease demonstrates about 1% or less of a normal α-L-iduronidase activity.

44. (New) The method of Claim 39 wherein a dose of at least about 125,000 units or 0.5 mg/kg of said human recombinant α-L-iduronidase is administered weekly to a patient suffering from a deficiency thereof.

45. (New) The method of Claim 39 wherein said administering is a slow infusion of at least 0.5 mg/kg of said formulation for about an hour, followed by a rapid two-hour infusion rate.

46. (New) The method of Claim 45 wherein said infusion is used to minimize complement mediation clinical allergic reactions.

47. (New) The method of Claim 39 wherein said administering with human recombinant α-L-iduronidase reduces lysosomal storage.

48. (New) The method of Claim 39 wherein said administering results in a decrease in the volume of the liver of said patient by at least 5%.

49. (New) The method of Claim 48 wherein said administering results in a decrease in the volume of the liver of said patient by at least 19%.

50. (New) The method of Claim 39 wherein said administering results in a decrease in the volume of the spleen of said patient by at least 13%.

51. (New) The method of Claim 39 wherein said administering results in a decrease in the urinary glycosaminoglycan excretion of said patient by at least 60%.

52. (New) The method of Claim 39 wherein said patient is a prepubertal patient and said administering results in an increase of the height growth velocity of said patient by at least 2.4 cm/year.

53. (New) The method of Claim 39 wherein said patient is a prepubertal patient and said administering results in an increase of the weight growth velocity of said patient by at least 2.4 kg/year.

54. (New) The method of Claim 39 wherein said administering results in an increase of the shoulder flexion of said patient.

55. (New) The method of Claim 39 wherein said administering results in an increase of the elbow and knee extension of said patient.

56. (New) The method of Claim 39 wherein said administering results in a reduction of apnea and hypopea events of said patient.

57. (New) The method of Claim 39 wherein said patient has tricuspid regurgitation or pulmonic regurgitation caused all or in part by a deficiency in α-L-iduronidase treatment and wherein said administering results in a reduction in said tricuspid regurgitation or pulmonic regurgitation.--